

# Integrated management of HIV, diabetes, and hypertension in sub-Saharan Africa (INTE-AFRICA): a pragmatic cluster-randomised, controlled trial



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## Summary

**Background** In sub-Saharan Africa, health-care provision for chronic conditions is fragmented. The aim of this study was to determine whether integrated management of HIV, diabetes, and hypertension led to improved rates of retention in care for people with diabetes or hypertension without adversely affecting rates of HIV viral suppression among people with HIV when compared to standard vertical care in medium and large health facilities in Uganda and Tanzania.

**Methods** In INTE-AFRICA, a pragmatic cluster-randomised, controlled trial, we randomly allocated primary health-care facilities in Uganda and Tanzania to provide either integrated care or standard care for HIV, diabetes, and hypertension. Random allocation (1:1) was stratified by location, infrastructure level, and by country, with a permuted block randomisation method. In the integrated care group, participants with HIV, diabetes, or hypertension were managed by the same health-care workers, used the same pharmacy, had similarly designed medical records, shared the same registration and waiting areas, and had an integrated laboratory service. In the standard care group, these services were delivered vertically for each condition. Patients were eligible to join the trial if they were living with confirmed HIV, diabetes, or hypertension, were aged 18 years or older, were living within the catchment population area of the health facility, and were likely to remain in the catchment population for 6 months. The coprimary outcomes, retention in care (attending a clinic within the last 6 months of study follow-up) for participants with either diabetes or hypertension (tested for superiority) and plasma viral load suppression for those with HIV (>1000 copies per mL; tested for non-inferiority, 10% margin), were analysed using generalised estimating equations in the intention-to-treat population. This trial is registered with ISCRTN 43896688.

**Findings** Between June 30, 2020, and April 1, 2021 we randomly allocated 32 health facilities (17 in Uganda and 15 in Tanzania) with 7028 eligible participants to the integrated care or the standard care groups. Among participants with diabetes, hypertension, or both, 2298 (75·8%) of 3032 were female and 734 (24·2%) of 3032 were male. Of participants with HIV alone, 2365 (70·3%) of 3365 were female and 1000 (29·7%) of 3365 were male. Follow-up lasted for 12 months. Among participants with diabetes, hypertension, or both, the proportion alive and retained in care at study end was 1254 (89·0%) of 1409 in integrated care and 1457 (89·8%) of 1623 in standard care. The risk differences were -0·65% (95% CI -5·76 to 4·46; p=0·80) unadjusted and -0·60% (-5·46 to 4·26; p=0·81) adjusted. Among participants with HIV, the proportion who had a plasma viral load of less than 1000 copies per mL was 1412 (97·0%) of 1456 in integrated care and 1451 (97·3%) of 1491 in standard care. The differences were -0·37% (one-sided 95% CI -1·99 to 1·26; p<sub>non-inferiority</sub><0·0001 unadjusted) and -0·36% (-1·99 to 1·28; p<sub>non-inferiority</sub><0·0001 adjusted).

**Interpretation** In sub-Saharan Africa, integrated chronic care services could achieve a high standard of care for people with diabetes or hypertension without adversely affecting outcomes for people with HIV.

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## Introduction

An estimated 2 million people die prematurely from the complications of hypertension or type 2 diabetes in sub-Saharan Africa,<sup>1,2</sup> and this figure is expected to rise sharply in the coming years. By contrast, HIV-associated

mortality, which peaked on the continent at over 2 million deaths a year in the early 2000s, has been declining and now causes fewer than half a million deaths a year.<sup>3</sup>

Across sub-Saharan Africa, HIV care is organised separately from other health service provisions. This

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## Research in context

### Evidence before this study

The burden of diabetes and hypertension has risen rapidly in sub-Saharan Africa, with about 2 million deaths now attributed annually to the effects of these conditions alone. This rise in mortality has occurred alongside a continuing high burden of HIV. Health-care services for chronic conditions other than HIV are generally fragmented. HIV care is provided through dedicated HIV clinics, with patients managed separately from those with other conditions. Services for diabetes and hypertension are not available from some primary health-care facilities on the same day. In some settings, diabetes care is available only from higher level facilities.

Literature searches were conducted at several points before the start of this trial. In preparation for the pilot study that preceded and informed the INTE-AFRICA trial design, a review of the literature, conducted in 2018, found several published studies and a systematic review of studies that had integrated hypertension, diabetes, or cardiovascular disease care into the HIV platform. Only one study, from Malawi, reported on a chronic care clinic that was built on an HIV platform but treated people who did not have HIV. This did not have a comparator group.

The literature search for trials of integrated care was done in PubMed and used the terms “sub-Saharan Africa” AND “integrated care” or “integration” OR “integrated” AND (“trials” OR “clinical trials” OR “RCT” OR “clinical trial[MeSH]” AND “HIV[MeSH Terms]” OR “HIV” OR “HIV care”). This was

repeated several times. The last search was done on Jan 13, 2020. We did not find any papers reporting on trials of integrated delivery of HIV and hypertension and diabetes care.

### Added value of this study

To our knowledge, this is the first randomised controlled trial to evaluate a fully integrated model of HIV, hypertension, and diabetes care in sub-Saharan Africa, including people with chronic conditions who do not also have HIV. To generate generalisable policy-relevant evidence, our study was randomised, large, and conducted in two countries (Tanzania and Uganda); more than 6000 patients who attended 32 health facilities were followed up for 12 months. The trial showed that integrated management resulted in a high rate of retention in care for people with diabetes, hypertension, or both conditions, did not adversely affect viral suppression rates among people with HIV, and was cost saving for health services.

### Implications of all the available evidence

The study provides clear evidence for policy makers to start to scale up integrated care for HIV, diabetes, and hypertension. As the burden of non-communicable conditions increases in sub-Saharan Africa, and more people require care for multiple conditions, integrated management is likely to be an essential and cost-effective approach for the continent. The study also serves as a proof-of-concept for integrated management more broadly, which will inform research and clinical practice in other parts of the world.

vertical approach started around 2003, following donor funding for antiretroviral therapy programmes, and continues today, despite 60% of the HIV response now being funded from domestic sources.<sup>3</sup>

The challenge of vertical care services is that they split health-care resources and cause inequity. For patients living with multiple chronic conditions, vertical services mean multiple visits to different clinics.<sup>4,5</sup> Health policies in sub-Saharan Africa now recommend integrated health-care provision,<sup>6,7</sup> but there is no published evidence from a randomised controlled trial to support this and so public health practice is unlikely to change. A major concern with integrated care is that reorganisation of HIV services to incorporate them into broader programmes could worsen HIV service provision and jeopardise the gains achieved by HIV programmes.

In a previous single-arm study conducted in Tanzania and Uganda, we showed that integrated management of HIV, diabetes, and hypertension was feasible,<sup>8</sup> generally liked by patients and health-care providers,<sup>9,10</sup> and was potentially cost-effective.<sup>11</sup> Here we present the findings from a large cluster-randomised trial comparing integrated management with standard vertical care. The trial was designed to test whether integrated

management was superior to standard care in terms of retaining people with diabetes, hypertension, or both conditions concurrently in care, and whether it was non-inferior in terms of viral suppression among people with HIV alone, when compared with standard vertical care.

## Methods

### Study design and participants

The INTE-AFRICA trial is a pragmatic multi-country, cluster-randomised, controlled trial, comparing provision of integrated care with standard vertical care delivered separately for people with HIV, diabetes, or hypertension.<sup>12</sup> It was conducted in 32 medium to large sized health facilities, located in largely urban and peri-urban settings in Dar es Salaam, Tanzania, and Kampala and the central and western regions of Uganda. The protocol was approved by ethics committees of The AIDS Support Organisation, Uganda; the National Institute of Medical Research, Tanzania; and the Liverpool School of Tropical Medicine, UK.

The protocol has been published previously.<sup>12</sup> Health facilities were eligible for inclusion in the trial if they provided dedicated care for diabetes and HIV infection in separate clinics. Exclusion criteria included facilities that did not provide specialist referral care and did not provide

diabetes services. Large hospitals that act as referral centres, selected specialist district hospitals, and small health facilities run by nurses and junior part-qualified doctors that do not provide either HIV, diabetes, or hypertension services, or facilities with a small patient volume, were also excluded.

Patients were eligible to join the trial if they were living with confirmed HIV, diabetes, or hypertension, were aged 18 years or older, were living within the catchment population area of the health facility, and were likely to remain in the catchment population for 6 months. Patients were excluded if they required immediate hospital care.

Each site had a high volume of patients attending with HIV or hypertension, and we used systematic sampling to screen them for eligibility. We approached every fifth or tenth patient, depending on the size of the clinic. Due to the lower number of patients with known diabetes or multiple conditions, we invited all to enrol consecutively. Patients were provided with written information about the study in their preferred language, and enrolled, following written informed consent, by trained research nurses.

### Randomisation

Random allocation was stratified by the location of the health facility (region and urban, peri-urban, or rural setting), infrastructure level of the health facility,<sup>8,12</sup> and by country. Within each stratum, facilities were randomly allocated in a 1:1 ratio to either integrated care or standard care using a permuted block randomisation method generated by PROC PLAN in SAS version 9.4. The randomisation list was generated by an independent statistician. Analyses were done masked to random allocation.

### Procedures

The trial was conducted in close-to-normal health service conditions, with government health-care staff treating study participants.<sup>12</sup> Health care provision, including the establishment of the integrated care clinics within the designated health facilities, was done by health-care services staff. Integrated clinics functioned as distinct and separate clinics at the health facilities.<sup>12</sup> We involved patients, health-care providers, civil society organisations, and local and national policy makers from the outset of protocol development, in defining the research questions, study design, implementation, and interpretation of findings.<sup>13</sup>

In the integrated care group participants with either HIV, hypertension, or diabetes attended a single clinic. They shared the same registration and waiting area, were managed by the same health-care workers, and used the same pharmacy. Their medical records were stored in folders with a similar appearance, to ensure a consistent approach to care across these conditions. Their laboratory services were also integrated.<sup>12</sup>

In the standard care group participants attended existing separate standalone clinics for either HIV or

diabetes or hypertension (ie, standard current practice across sub-Saharan Africa). Registration, waiting areas, clinical management, pharmacies, and laboratory testing were all provided separately.<sup>12</sup>

Clinics providing diabetes and hypertension care generally did not keep medical records. The research team assisted all health facilities in the trial to introduce both medical records and active tracing of patients with these conditions.<sup>8,12</sup> Patients who missed appointments were contacted by health facility staff (by telephone or very rarely by home visit, with the first attempt within a week of a missed appointment) and were encouraged to attend clinic. At least three attempts were made before a patient was declared lost to follow-up. Medical records and active tracing were already standard practice in HIV clinics.

A major challenge was that shortages in medicines for diabetes and hypertension were common in the health facilities.<sup>14</sup> The research programme provided a buffer supply of medicines to the health facilities for the first 2 months.<sup>8,9</sup> In addition, in Uganda, we enabled patients to contribute money into a single fund and purchase drugs in bulk for use when government supplies were limited. In Tanzania, patients typically paid for their care, or had insurance plans that covered the costs, and the health facilities prioritised provision of medicines for those who had no insurance and were not able to pay.

Research data collection was done by trained researchers at baseline and months 6 and 12. We recorded all attendances, and transcribed data from medical records attendances that occurred at other times (eg, unscheduled attendances). Where needed, the research programme contributed to the cost of the laboratory tests and supplied materials for conducting tests for the trial endpoint assessments.

Retention was assessed through routine attendance at clinics and through the track-and-trace procedures implemented by health facilities. A participant was regarded as lost to follow-up if they had not attended an appointment within the previous 6 months.

Blood pressure was measured using the Omron M6 comfort (OMRON Healthcare; Den Bosch, Netherlands) in both Uganda and Tanzania. We measured blood pressure at two timepoints on the left arm with the participant in the sitting position, 5 min apart, and took the average of the two readings as the pressure. Hypertension was defined as any one of the following, alone or in combination: a systolic pressure of 140 mm Hg or higher, a diastolic pressure of 90 mm Hg or higher, or the use of antihypertensive medications.

Plasma viral load testing was done by the Central Public Health laboratories in Tanzania and Uganda using the Cobas 8800 system (Roche Diagnostics, Johannesburg, South Africa). Fasting blood glucose was done at the health facilities using a point of care test kit (HemoCue Glucose 201 RT Hemocue AB [Angelholm, Sweden]) in Tanzania and Contour Plus (Bayer [Leverkusen, Germany]) in Uganda.

In Tanzania, weight and height were measured using SECA RGZ-160 (SECA, Hamburg, Germany). In Uganda, SECA 876 was used for weight measurement and SECA 213 portable stadiometer (both SECA, Hamburg, Germany) for height measurement. Weight and height were measured to the nearest 0.1 kg and 0.1 cm, respectively, and BMI was calculated as kg/m<sup>2</sup>. This was used as a baseline indicator to describe the population.

### Outcomes

The study had two coprimary endpoints: retention in care for participants with either diabetes or hypertension (tested for superiority of integrated care) and plasma viral load suppression for those with HIV (tested for non-inferiority).<sup>12</sup> Retention in care was chosen as a primary endpoint, as the loss from care is probably the biggest determinant of mortality among people with diabetes or hypertension, and the immediate problem that policy makers wanted to address. Secondary endpoints were blood pressure and glycaemia control, rates of retention for all patients, and costs of care.

The independent data monitoring committee met at the beginning of the trial and once during the study period. The Trial Steering Committee met approximately once every 6 months, and also had oversight of the trial. Safety was assessed in the intention-to-treat population.

### Statistical analysis

We assumed that retention in care would be 60% in the standard care group.<sup>8,12,15</sup> With 32 health facilities, 100 participants with diabetes or hypertension in each facility and an intra-class coefficient of 0.06,<sup>16</sup> the trial had 90% power to detect an absolute difference of 15% between the study groups at the 5% two-sided significance level (ie, a retention of 60% versus 75% in the standard care and integrated care groups respectively).

We planned to enrol a similar number of participants with HIV, and had 90% power to show non-inferiority in plasma viral load suppression between the intervention group and standard care group with a 10% non-inferiority margin (ie, that the upper limit of the one-sided 95% CI of the difference between the two groups does not exceed 10%). This assumed an intra-class coefficient of variation of 0.06 and one-sided 95% CI.

General estimating equation models were used for the analysis to take account of clustering of data within health facilities. We used a binomial distribution and identity link function with the clinics (intervention *vs* control) as predictor, and clinic as cluster effect, to generate the risk differences, two-sided 95% CIs, and *p* values. In the adjusted analyses of the primary endpoints, we included the following: participant age, sex (from medical records), presence of comorbidity (any of HIV, diabetes, or hypertension) and location of trial site (urban, peri-urban, or rural setting) as covariates. The primary analysis for the coprimary endpoints was in

the intention-to-treat population. No adjustment for multiple comparisons was made, as the primary endpoints were from different patient populations.

We defined a participant as being retained in care if they were alive and in care, attended a clinic for their routine assessment within 6 months of enrolment and, at any time after that, that they had not been declared lost to follow-up, withdrawn, or dead. We anticipated that the largest losses from care would occur in the first 6 months, based on our previous research in this population and a systematic review.<sup>8,17</sup> At the time that this trial started, patients living with HIV were being followed up every 3–6 months. Those with diabetes or hypertension were usually seen more often, typically monthly.

HIV viral suppression was defined as a viral load of less than 1000 copies per mL (or reported as undetectable viral load).<sup>18</sup> Any viral load measurement taken at month 6 or later after enrolment in the trial was used in the endpoint analysis.

The primary efficacy analysis included participants with diabetes, hypertension, or both conditions concurrently for the retention in care endpoint, and participants with HIV alone for the viral suppression endpoint. The health economic analysis included all participants (ie, any combination of HIV, diabetes, or hypertension).

We conducted a provider perspective economic evaluation to estimate the average monthly cost per patient for the trial population. Personnel and overhead costs were estimated using a top-down approach,<sup>11</sup> while medication and diagnostic costs were estimated using a bottom-up approach.<sup>19</sup> All costs are reported in 2021 international dollars (Int\$). More details on the economic evaluation methods, resources considered, and prices used are included in the appendix pp 11–13. The data monitoring committee is listed in the protocol. The trial was registered with the International Standard Randomised Controlled Trial Number registry, ISRCTN43896688.

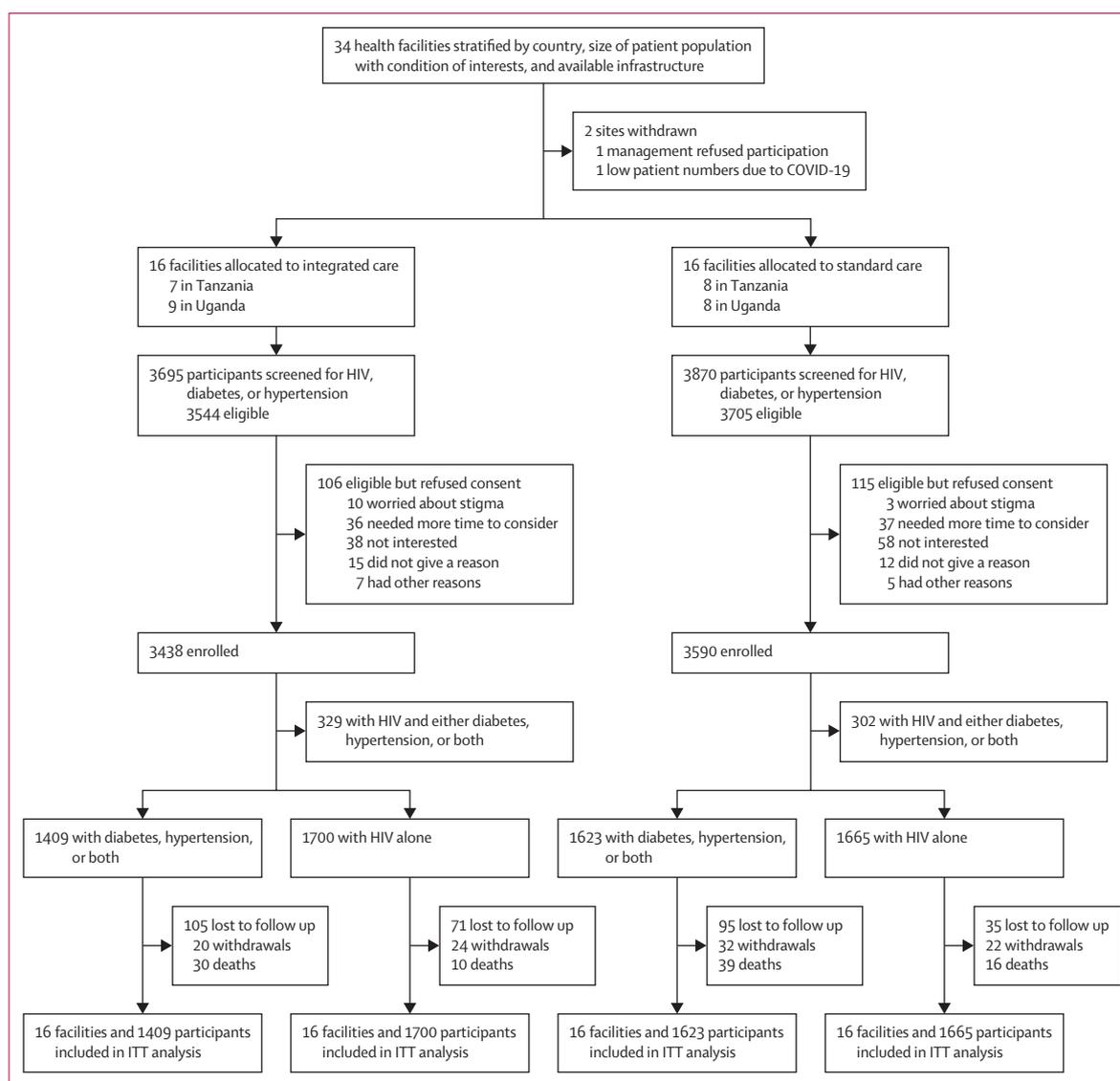
### Role of the funding source

The funders had no role in data collection, analysis, interpretation of the findings, writing of the paper, or the decision to submit.

### Results

Between June 30, 2020, and April 1, 2021, we screened 3543 patients attending a diabetes or hypertension clinic and 4023 attending an HIV clinic in 17 health facilities in Uganda and 15 health facilities in Tanzania (figure). Overall, 7249 (96.0%) of 7565 patients were eligible for the study (figure) and 106 (3.0%) of 3544 in the integrated care group and 115 (3.1%) of 3705 in the standard care group declined to join. Of the 7028 enrolled, 3032 (43.1%) had diabetes alone, hypertension alone, or both diabetes and hypertension, and 3365 (47.9%) had HIV alone. These populations are the basis of this report, as

See Online for appendix



**Figure: Trial profile**  
ITT=intention-to-treat.

pre-specified in the statistical analysis plan. A further 94 (1.3%) of 7028 participants had concomitant HIV and diabetes, 454 (6.5%) of 7028 had HIV and hypertension, and 83 (1.2%) of 7028 had HIV, diabetes, and hypertension, and are not part of the analyses on efficacy, but they were included in the health economics analyses. In the appendix, we provide results on the entire cohort, including these participants (p 2).

Baseline characteristics of participants were balanced between groups and are shown in table 1. 4663 (72.9%) of 6397 were women and 1734 (27.1%) were men. The rates of blood pressure or glycaemia control were low while the rates of HIV viral suppression were high.

The median follow-up of the cohort was 12.5 months (IQR 11.9–13.6) in the integrated care group and 12.5 months (11.9–13.5) in the standard care group. The

proportion of participants with either diabetes, hypertension, or both who were alive and retained in care at the end of the study was 1254 (89.0%) of 1409 in the integrated care group and 1457 (89.8%) of 1623 in the standard care group (table 2). The risk difference between the two groups was not significant (−0.65%, 95% CI −5.76 to 4.46;  $p=0.80$  from crude analysis and −0.60%, −5.46 to 4.26;  $p=0.81$  from adjusted analysis for integrated care minus standard care).

We had 22 protocol deviations recorded: in nine cases, the site that the participant was enrolled was recorded incorrectly, seven participants were enrolled twice (and duplicated records were removed) and five participants did not complete a final short questionnaire on their family history and basic knowledge of the chronic conditions.

	Participants with diabetes, hypertension, or both		Participants with HIV alone	
	Integrated care (n=1409)	Standard care (n=1623)	Integrated care (n=1700)	Standard care (n=1665)
<b>Site</b>				
Tanzania	544 (38.6%)	803 (49.5%)	880 (51.8%)	830 (49.8%)
Uganda	865 (61.4%)	820 (50.5%)	820 (48.2%)	835 (50.2%)
<b>Condition</b>				
Diabetes alone	180 (12.8%)	307 (18.9%)	NA	NA
Hypertension alone	906 (64.3%)	883 (54.4%)	NA	NA
Diabetes and hypertension	323 (22.9%)	433 (26.7%)	NA	NA
HIV alone	NA	NA	1700 (100.0%)	1665 (100.0%)
Years living with condition, median (IQR)	3.0 (1.0–6.0)	3.0 (1.0–.0)	5.4 (2.6–8.5)	5.6 (2.6–9.0)
<b>Sex</b>				
Female	1092 (77.5%)	1206 (74.3%)	1230 (72.4%)	1135 (68.2%)
Male	317 (22.5%)	417 (25.7%)	470 (27.6%)	530 (31.8%)
<b>Education</b>				
No formal education	393/1408 (27.9%)*	280 (17.3%)	289 (17.0%)	166 (10.0%)
Primary school	748/1408 (53.1%)*	1024 (63.1%)	1076 (63.3%)	1198 (72.0%)
Secondary or tertiary	267/1408 (19.0%)*	318 (19.6%)	335 (19.7%)	301 (18.1%)
<b>Age, years</b>				
Mean, SD	60.1 (12.7)	57.7 (12.2)	42.6 (11.2)	42.7 (10.8)
<35	43 (3.1%)	60 (3.7%)	441 (25.9%)	405 (24.3%)
35–49	261 (18.5%)	341 (21.0%)	826 (48.6%)	861 (51.7%)
≥50	1105 (78.4%)	1222 (75.3%)	433 (25.5%)	399 (24.0%)
<b>BMI, kg/m<sup>2</sup></b>				
<25.0	551 (39.1%)	645 (39.7%)	1051 (61.8%)	1088 (63.4%)
25.0–29.9	456 (32.4%)	551 (33.9%)	391 (23.0%)	367 (22.0%)
≥30.0	402 (28.5%)	427 (26.3%)	258 (15.2%)	210 (12.6%)
<b>Blood pressure</b>				
<140/90 mm Hg among participants with hypertension	496/1229 (40.4%)	421/1316 (32.0%)	..	..
<b>Fasting blood glucose</b>				
6.9 mmol/L among participants with diabetes	111/391 (28.4%)†	140/670 (20.9%)‡	..	..
<b>HIV viral load</b>				
<1000 copies per mL	..	..	1547/1618 (95.6%)§	1539/1631 (94.4%)¶
<400 copies per mL	..	..	1438/1618 (88.9%)§	1409/1631 (86.4%)¶

Data are n (%) unless otherwise stated. Some totals may not equal 100% owing to rounding. NA=not applicable. \*Missing for one participant. †Missing for 112 participants. ‡Missing for 70 participants. §Missing for 83 participants. ¶Missing for 34 participants. These data were missing usually because the participant had not fasted, or the clinic was busy and overlooked doing the sample viral load testing.

Table 1: Baseline characteristics

The proportion retained in care who transferred to another facility included 20 (1.4%) of 1410 participants in the integrated care group and eight (0.5%) of 1623 in the standard care group. If they are considered as lost to follow-up, then the retention rate becomes 1234 (87.6%) of 1409 in the integrated care group and 1449 (89.3%) of 1623

in the standard care group (risk difference  $-1.55\%$ , 95% CI  $-7.07$  to  $3.97$ ;  $p=0.58$ , from crude analysis and  $-1.26\%$ ,  $-6.51$  to  $3.98$ ,  $p=0.64$  from adjusted analysis; appendix p 2). Findings from the per protocol analyses (appendix p 5) and from the within group analyses (appendix pp 6–7) were similar.

Blood pressure and glucose indicators were all improved in the integrated care group compared with standard care, but were statistically significant only for the change in blood glucose from baseline (table 1).

The retention rate of participants with HIV was also high (table 3). The proportion of participants with HIV viral suppression (defined as  $<1000$  copies per mL) at the study end exceeded 95% in both groups. The differences in the proportion of participants with viral suppression between the two groups was  $-0.37\%$  (one-sided 95% CI  $-1.99$  to  $1.26$ ;  $p_{\text{non-inferiority}} < 0.0001$ ) unadjusted and  $-0.36\%$  ( $-1.99$  to  $1.28$ ;  $p_{\text{non-inferiority}} < 0.0001$ ) adjusted. The lower limit of the one-sided 95% confidence interval in the difference was thus above  $-10\%$ , the prespecified non-inferiority margin, and the statistical test of whether non-inferiority was established was  $p < 0.0001$ . If all participants in whom plasma viral load was not measured are assumed to have viral load exceeding 1000 copies per mL, the proportion with HIV viral suppression was 1412 (83.1%) of 1700 in the integrated group and 1451 (87.1%) of 1665 in the standard care group (adjusted difference  $-5.9$ , 95% CI  $-13.1$  to  $1.4$ ;  $p=0.11$ ). Findings from the per protocol analyses were similar (appendix p 6).

Rates of participants with diabetes, hypertension, or both and with HIV viral suppression who were alive and retained in care were similar between male and female participants (appendix p 8). Overall, among participants with diabetes, hypertension, or both, who had no complications at baseline, there were 95 episodes of new clinical complications (6.7%) of 1409 in the integrated care group and 102 episodes (6.3%) of 1623 in standard care (appendix p 3). These figures for the participants with HIV were 17 episodes (1.0%) of 1700 and 24 episodes (1.4%) of 1664, respectively (appendix p 4).

Costs did not differ substantially between the two groups for participants with single conditions. In both countries, the average monthly provider cost per participant with multiple conditions in the integrated care group was lower in almost all circumstances than in the standard care group (table 4). Savings were driven by reduced staffing and overhead costs associated with the reduced number of total visits required by patients with multiple morbidities in the integrated care group, compared with standard care. Cost savings through integrated care were primarily driven by efficiency gains in how patients with multiple morbidities were managed in facilities (appendix pp 13–17). The number of staff, and associated staff contact time, was lower in integrated care, as a single clinician could provide care to patients with multiple morbidities, compared with the requirement for several physicians in vertical care.

Patients in integrated care also used less of the facility surface area, such as waiting areas and clinician offices, resulting in lower overhead costs in integrated care (lower rental costs, as smaller clinics can provide equivalent services, and associated lower maintenance costs) compared with vertical care.

## Discussion

This trial demonstrated that integrated chronic care management in a sub-Saharan African health care setting was associated with a high level of retention in care for people with diabetes or hypertension, although not superior to vertical management, and that integration did not adversely affect the rate of viral suppression among people with HIV.

To our knowledge, this is the first rigorous study of its kind from a low-income setting where an integrated model of care for people with different chronic conditions has been tested. Previous studies have been mostly small and non-randomised, and have tested simple models of expanding HIV services to manage non-communicable conditions among people with HIV,<sup>20–26</sup> which does little for people with chronic conditions who do not have HIV.

In previous studies, retention in care of patients with diabetes or hypertension has rarely exceeded 50%, even in settings where there was access to good clinical care.<sup>8,17,27–32</sup> We believe that there are two factors that led to the very high retention levels (over 89% in both groups) observed in our trial.

First, health services introduced information and adherence counselling for participants with diabetes or hypertension in both groups. Participants who missed appointments were traced actively and encouraged to attend their clinic, which has been standard policy in HIV care across sub-Saharan Africa since the expansion of antiretroviral therapy services.<sup>33–36</sup>

Second, we conducted extensive engagement with our stakeholder community. We had learnt from our pilot study<sup>8</sup> on how to communicate the effects of diabetes and hypertension with patients. Experienced health facility and research staff gave structured health talks on these conditions and on this study's aims. These talks involved the patients and anyone at the health facility that the patient might come in contact with, from the receptionist to the senior doctors. The talks were done in both groups. We also involved senior disease control managers, and local and national policy makers, meeting with these groups every 3–6 months. Senior policy makers visited the research sites periodically and engaged directly with health-care staff and patients. We conducted the stakeholder engagement before and during the trial, and after the trial ended.

What this suggests is that small changes to non-communicable disease programmes, taken from the experiences gained in HIV control, combined with relatively small investments and the involvement of the different stakeholders as partners, could have a major

	Integrated care (n=1409)	Standard care (n=1623)	Crude risk or mean difference (95% CI)*	Adjusted risk or mean difference (95% CI)†
<b>Primary outcome</b>				
Retention in care	1254 (89.0%)	1457 (89.8%)	-0.65 (-5.76 to 4.46); p=0.80	-0.60 (-5.46 to 4.26); p=0.81
<b>Secondary outcomes</b>				
Blood pressure control among participants with hypertension				
Blood pressure <140/90 mm Hg	588/1044 (56.3%)	581/1230 (47.2%)	8.66 (-1.00 to 18.32); p=0.079	8.14 (-0.58 to 16.87); p=0.067
Change in systolic blood pressure from baseline in mm Hg (mean [SD])	1044 (-5.75 [22.39])	1230 (-2.66 [21.70])	-3.96 (-5.45 to -2.48); p<0.0001	-3.15 (-6.46 to 0.16); p=0.062
Change in diastolic blood pressure from baseline in mm Hg (mean [SD])	1044 (-2.51 [12.82])	1230 (-2.52 [13.41])	-1.42 (-2.29 to -0.54); p=0.0015	-1.17 (-2.98 to 0.63); p=0.20
Blood glucose control among participants with diabetes				
Fasting blood glucose 6.9 mmol/L	49/190 (25.8%)	94/467 (20.1%)	5.78 (-1.30 to 12.87); p=0.11	4.50 (-1.57 to 10.58); p=0.15
Change in fasting blood glucose from baseline (mean [SD])	151 (-1.15 [6.61])	409 (-0.10 [5.23])	-1.04 (-1.87 to -0.22); p=0.013	-1.14 (-2.02 to -0.26); p=0.011
Either blood pressure <140/90 mm Hg or fasting blood glucose 6.9 mmol/L	612/1046 (58.5%)	627/1246 (50.3%)	8.34 (-1.32 to 18.00); p=0.091	8.09 (-0.37 to 16.55); p=0.061

Data are n (%) or n/n with available data unless otherwise stated. \*Adjusted for clustering and baseline measurement for a continuous outcome. †Adjusted for clustering, age, sex, comorbidity, and location (rural, peri-urban, urban). The blood pressure and glucose measurements are also adjusted for baseline measurements of these variables.

Table 2: Trial outcomes in participants with diabetes, hypertension, or both

	Integrated care (n=1700)	Standard care (n=1665)	Crude risk difference (95% CI); p value	Adjusted risk difference (95% CI); p value*
<b>Primary outcome</b>				
Plasma viral load <1000 copies per mL	1412/1456 (97.0%)	1451/1491 (97.3%)	-0.37 (-1.99 to 1.26); p<0.0001†	-0.36 (-1.99 to 1.28); p<0.0001†
<b>Secondary outcomes</b>				
Alive and retained in care	1595 (93.8%)	1592 (95.6%)	-2.12 (-4.58 to 0.34); p=0.092	-2.30 (-4.62 to 0.03); p=0.053
Plasma viral load <400 copies per mL	1358/1456 (93.3%)	1400/1491 (93.9%)	-1.25 (-4.72 to 2.23); p=0.49	-0.69 (-3.50 to 2.11); p=0.63
Achieved viral suppression (<1000 copies per mL) while on the trial	46/1408 (3.3%)	58/1483 (3.9%)	-0.58 (-2.69 to 1.53); p=0.67	-0.19 (-2.31 to 1.94); p=0.95

Data are n/N with available data or n (%), unless otherwise stated. \*Adjusted for clustering, age, sex, comorbidity, and location (rural, peri-urban, urban). †One-sided 95% CI was calculated. p value from non-inferiority test.

Table 3: Trial outcomes among participants with HIV alone

effect on the long-standing seemingly intractable problem of poor retention in care in non-communicable disease programmes in sub-Saharan Africa, whether or not services are integrated.

	Uganda			Tanzania		
	Integrated care, mean (SD)	Standard care, mean (SD)	Mean difference in cost (95% CI); p value*	Integrated care, mean (SD)	Standard care, mean (SD)	Mean difference in cost (95% CI); p value*
HIV alone	67.33 (16.67)	70.33 (18.61)	3.00 (1.20 to 4.80); p<0.0005	60.08 (9.22)	59.62 (9.77)	-0.46 (-1.39 to 0.47); p=0.16
Hypertension alone	56.07 (17.40)	57.25 (21.39)	1.18 (-1.34 to 3.71); p=0.18	18.72 (6.85)	16.54 (6.45)	-2.18 (-3.16 to -1.21); p<0.0001
Diabetes alone	50.15 (20.06)	42.51 (19.53)	-7.64 (-13.36 to -1.93); p=0.0045	19.99 (8.47)	16.95 (8.71)	-3.05 (-5.60 to -0.49), p=0.0098
HIV and hypertension	81.16 (18.57)	120.65 (40.51)	39.49 (32.27 to 46.72); p<0.0001	62.58 (10.47)	72.92 (14.22)	10.34 (7.62 to 13.06); p<0.0001
HIV and diabetes	90.17 (11.66)	112.83 (53.3)	22.66 (-6.19 to 51.52); p=0.059	62.88 (12.07)	72.61 (22.98)	9.73 (0.31 to 19.76); p=0.029
Hypertension and diabetes	57.84 (17.59)	100.70 (41.83)	42.86 (37.08 to 48.64); p<0.0001	28.97 (9.81)	37.38 (16.20)	8.41 (4.98 to 11.84); p<0.0001
HIV, hypertension, and diabetes	106.02 (29.74)	174.30 (60.92)	68.28 (38.22 to 98.33); p<0.0001	71.26 (13.42)	91.24 (26.81)	19.98 (8.66 to 31.30); p=0.0004

\* Average difference in costs, two-sided test at a 5% significance level.

**Table 4: Average monthly provider cost per patient in 2021 international dollars, stratified by country and study group**

Although in our trial some measures of blood pressure and glycaemia were superior in the integrated care group than in standard care, barely half of the participants with hypertension and one quarter with glycaemia reached target levels. Control of blood pressure and glycaemia are a challenge globally,<sup>37-39</sup> but in low-income African settings, retaining people in care but not controlling their blood pressure and glycaemia adequately will not be sustainable. A priority now is to identify interventions that will improve control of these conditions in sub-Saharan Africa.

While it was essential to leverage the learning and experiences of HIV programmes,<sup>25,40</sup> our biggest concern was that the reorganisation of care into integrated care clinics would have a detrimental effect on HIV outcomes. Our study shows convincingly that this was not the case, with rates of HIV viral suppression that exceeded 95% in both groups at 12 months using our model of integrated care. Social science investigations suggested that integrated care improved the patient experience and did not increase stigma.<sup>10,41</sup>

We also showed that the integrated model of care was cost saving for the health services for participants with multiple conditions compared with participants using single clinics. Data on the prevalence of multiple chronic conditions in sub-Saharan Africa are scarce, but globally we know that one in three adults are living with multiple conditions,<sup>42,43</sup> and so the potential cost savings for health services of moving to integrated care could be substantial.

The study was large, done in close-to-normal health service conditions and with replication across different settings to increase generalisability. A limitation was that participants in the integrated care group could withdraw from the study and continue to receive standard care from the same health facility, thus having a choice of two models of care. In the standard care group participants

who withdrew continued to receive standard care, but had no further contact with the research team. Thus, we might have underestimated retention in care in the integrated care group.

Control of hypertension and diabetes in sub-Saharan Africa has been a huge challenge. We are probably where we were with HIV control in sub-Saharan Africa 20 years ago, but face a bigger challenge going forward, as the burden of non-communicable conditions is very high. Our research shows a pathway for tackling these conditions and bringing down their associated mortality, while maintaining good outcomes for people with HIV.

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**Contributors**

SK and JB coordinated the trial, supervised by SM, KR, MJN, and KM, and were supported by JO, SA, FT, SO, IN, and MS. DW and JO verified the data and did the statistical analysis. EvW managed the data. JS, GAJ, NB, and CJ did the health economic analysis. GM, JM, MNS, BME, OSU, AM, and SW contributed to defining the research question, and supporting the implementation and interpretation of the findings. MJN, SM, and SJ designed the study and wrote the proposal for funding, supported by AG, LC, NKS, GG, AK, PGS, MB, and JVL. NKS, GG, AK, and PGS supervised the study. SK, JB, and JO wrote the first draft of the paper. SJ wrote subsequent drafts with inputs from the other authors. DW, EvW, JO, SK, JB, MN, SM, and SJ had full access to the data. All authors saw and agreed the final draft. SJ was responsible for submitting the paper.

**Declaration of interests**

We declare no competing interests.

**Data sharing**

Individual participant data that underlie the results reported in this article are available, after deidentification, to researchers who provide a methodologically sound proposal. Proposals should be directed to s.jaffar@ucl.ac.uk. Data will be available for 5 years. The study protocol, statistical analysis plan, and analytic code are available upon request. Source code for software used in the trial is publicly available at <https://github.com/inte-africa-trial/inte-edc>.

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